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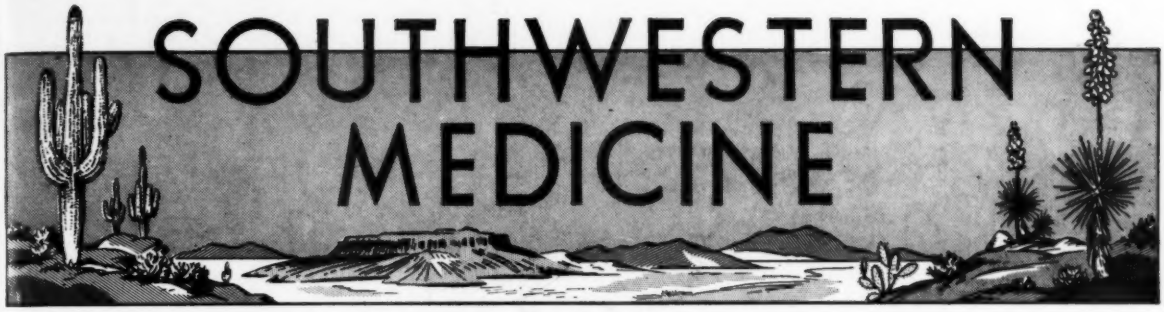

Volume XXVII EL PASO, TEXAS, AUGUST, 1943 Number 8

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Official Journal of
Arizona State Medical Association *New Mexico Medical Society*
El Paso County (Texas) Medical Society
Southwestern Medical Association

Such language!

My boss used to be as grumpy as a bear. He'd growl and bang around and his wife said: "Poor George, he's working too hard. It's wearing him down to a frazzle!"

So, I told her a few plain facts:

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When I had finished, she said she would certainly speak to George about using S-M-A as a routine formula.

* * *

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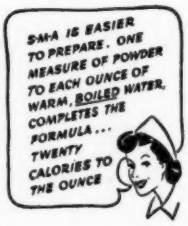
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SOUTHWESTERN MEDICINE

Vol. XXVII August, 1943 No. 8

OFFICIAL JOURNAL
Arizona State Medical Association
New Mexico Medical Society
Southwestern Medical Association
El Paso County (Texas) Medical Society

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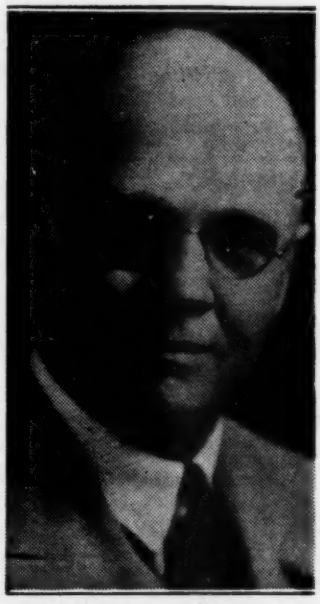
Two dollars per year 25c single copy

Entered at the postoffice at Phoenix, Arizona, as second-class matter.
Acceptance for mailing at special rate of postage provided for in section 1103. Act of October 3, 1917, authorized March 1, 1921.

ADVERTISING and SUBSCRIPTION OFFICES
A. C. Taylor Printing Company
142 South Central Avenue
Phoenix, Arizona

Eastern Representative:
Cooperative Medical Advertising Bureau
535 N. Dearborn St., Chicago



ORVILLE H. BROWN, M. D.

Dr. Orville Harry Brown, formerly of Phoenix, died July 25 in Arcadia, California, at the age of 68.

Dr. Brown retired from the active practise of medicine in Phoenix in 1940 and moved to California to reside with a daughter, Mrs. Harold Roach. For the past several years Dr. Brown has bravely and cheerfully carried on in the face of an incurable and painful disease.

Born in Brown County, Kansas, Dr. Brown's education was received at the University of Kansas, University of Chicago and St. Louis University. He took his M. D. degree from the latter institution in 1905. The early years of his practise were spent in St. Louis, where he filled the position of Assistant Professor of Medicine at St. Louis University. In 1916 Dr. Brown moved to Phoenix, where he entered the private practise of medicine, specializing in internal medicine.

Dr. Brown was a member of the American Medical Association, the Arizona State Medical Association, and the Southwestern Medical Association. He was a diplomate of the American Board of Internal Medicine and a fellow of the American College of Physicians, besides belonging to the American Association of Biological Chemists and the Royal Society of Medicine (London).

Dr. Brown wrote many articles for the medical literature. He was the author of a textbook on asthma and another on laboratory physiology.

For several years he was editor-in-chief of Southwestern Medicine. During his tenure he enlivened the pages of this Journal with numerous straight-hitting editorials. In these writings he displayed the characteristic of eternally hammering at what he conceived to be the truth, regardless of whether his attitudes and concepts might be popular or not. He was a man of gentleness, tolerance and high understanding. His opinion was respected and sought in the councils of organized medicine in the entire Southwest. He was a leader in medical and likewise in civic endeavors. He often inspired younger physicians to emulate his habits of observation and deduction.

Dr. Brown occupied a high place in the affections of this writer. He will be missed by hundreds of us in the medical profession of the Southwest. God grant this good man his well deserved peace and rest.

NEW MEDICAL JOURNALS

In all the present welter of hundreds of medical journals there are plenty that are simply money-making schemes that depend upon the high pressure selling tactics of a smooth-talking

ad peddler. In this category may be listed the throw-outs and the ambitious little sheets filled with sanitarium advertisements. Much has been said about these organs of paper wasting. So that here we will simply state it as an opinion that most of these promotion sheets have no reason at all for existing save to make profits for a promoter.

It is refreshing to note that two new journals of worth have recently been established by highly competent editorial boards. These journals are quarterly reviews. It appears that a series will eventually be placed in publication which will be concerned with the various specialties of medicine. The Quarterly Review of Otorhinolaryngology has been in existence for over a year. It is ably edited and is an extremely valuable journal. Now comes the Quarterly Review of Obstetrics and Gynecology, published at 314 Randolph Place, Northeast, Washington, D. C. The foreward of the first issue expresses ably the especial value of this new publication. It is hereby quoted:

"There has long been need for an abstract journal of Obstetrics and Gynecology in the English language. Such a periodical serves several purposes. In the first place it calls to the notice of the reader a vast array of articles which he would otherwise miss; and some of these he may find of special interest and value. Secondly, if the papers are well selected and comprehensively abstracted, a publication of this kind is a valuable time saver,—surely no small consideration in these hurried days when the pressure of practice leaves little time for medical literature. Finally, the bound volumes of an abstract journal, when properly indexed, constitute a most useful reference work in which the whole recent literature on any given subject may be reviewed in sequence.

"That great and scholarly German abstract journal, 'Berichte uber die Gesamte Gynakologie und Geburtshilfe,' which covered not only obstetrics and gynecology but certain related fields, was for many years a model of its kind. This is no longer available and it will doubtless be many years (if ever) before it attains its pre-war calibre; moreover, even in its prime the Berichte could be found in only a few of the larger medical libraries in this country and reached but a handful of American practitioners. It is particularly fitting, therefore, that an abstract journal in the English language be launched. The Quarterly Review of Obstetrics and Gynecology represents a beginning in this direction. It is hoped that successful issues will cover an increasing number of articles and that with the post-war period each issue will provide a comprehensive and up-to-the-minute survey of the entire world's literature in this field."

From personal experience with the Quarterly Review of Otorhinolaryngology this writer feels that the new quarterly review will more than adequately take the place of numerous other journals coming to the desk of the busy practitioner of obstetrics and gynecology. It is a distinct pleasure to endorse this new venture in medical journalism.

ABORTION

The whole question of abortion, therapeutic or elective, has been so shaded through the years by prejudices, taboos and unrealistic notions that it has been exceedingly difficult to shed light in this place where illumination is so badly needed. With the advent of the present regime in Russia there appeared an astonishing liberalism in that country regarding abortion. Here at least the pendulum swung completely across the arc from the point of thinking adopted by most of the rest of the civilized world. Of recent years, however, regarding mortality and morbidity rates of the woman subjected to unnatural deliverance of her child, there has been a marked reversal in attitude on the part of both the medical profession of Russia and the Government. Every physician knows that abortion does constitute a difficult and undeniable problem. The responsible, that is to say the majority element of American medicine, have decided, quite apart from the Hippocratic oath, that they want no part of the business. To the continuing shame of American medicine, however, here remain a few anti-social persons with medical training who even today engage in the wholesale murder of mothers and their unborn infants. Since the problem does exist and must be faced it would appear that no one could quarrel with the application of just plain common sense to the question. Recently the commitee on Maternal and Child Welfare of the Maine Medical Association published in the Journal of the Maine Medical Association an article unique in its exhibition of strong, good

Yankee common sense. The article is worth wide distribution. Here it is:

"Abortion is the cause of 25% of all maternal deaths in this country, the cause of 50% of all deaths attributed to puerperal sepsis. Dunn (Chief Statistician of the Bureau of Vital Statistics, Washington) states that between three and four thousand women die annually in the United States following abortion. Taussig estimates that 700,000 women each year undergo some type of abortion. A pool of available statistics indicates that 20%-30% of all pregnancies in cities and 5%-15% in rural districts are terminated prior to the period of viability. Of these abortions 33%-66% are induced. (The latter figure was derived from a questionnaire sent to Maine physicians and cited in the Encyclopedia of Social Sciences.) Since spontaneous abortions are seldom fatal and therapeutic abortions very rarely so, the vast majority of abortions that give rise to mortality statistics are illegally induced.

"The above figures demonstrate the seriousness of the abortion problem in this country. If illegal abortion could be done away with our maternal mortality would immediately be reduced by one-quarter. At least one thousand women who will be dead at the end of 1943 would then be alive. These women are not predominately 'unfortunate girls' who take this way to avoid the shame of illegitimate birth, they are not 'immoral women' who wish to rid themselves of the incumbrance incidental to their sinful mode of life. To the contrary 80%-90% of them are 'respectable married women' who have already borne children and who are impelled largely by economic motives to take this means of limiting their families.

"The average ethical physician views the question of abortion with mingled fear and indifference. His fear is a wholesale horror of becoming in anyway, however, innocently, associated with an abortion case. Should his name be so associated his professional reputation might well be jeopardized. His indifference is an outgrowth of the same fear. He knows nothing about abortion because he does not wish to know anything. In medical school we were warned to be always on our guard to avoid the suspicion of evil, we were told of the tricks that women sometimes employ to trap the unwary young physician into performing an abortion unwittingly. We were taught very little else on the subject. Our first impulse when a woman broaches the question of the interruption of pregnancy is to get her out of the office as fast as possible. We don't care where she goes as long as she gets out. This fact is so well known that few women would think of asking their family physicians about abortion. The woman who is unwillingly pregnant discusses the fact with her bosom friends and can usually find one who is only too pleased to direct her to some quack who proceeds to mutilate her and, now and then, to kill her.

"We would be the last to encourage the family physician to be more lenient on the subject of abortion. Our plea is for him to be less so. Not only to recoil in horror from performing an illegal abortion himself, but to take more active steps to prevent his patients from falling into the hands of those who do so. The woman who hysterically declares that she will not have a child (or another child) and that she is ready to take desperate measures to get rid of it is in dire need of guidance. If she is coldly shown the door she will probably rush out and do herself an injury or, more likely, pay someone else to do it. If she receives sympathy for her misfortune but is sadly told that the doctor can do nothing about it the result will be the same. If he tells her she will be doing wrong, that she will be liable to arrest, and that she may die she will answer that she considers it wrong to bring a child into the world that she cannot properly care for (meaning anything from feeding it to giving it a college education, according to her standard of living) and she will add dramatically that she would rather die than have this baby. She will half believe her own statements and again the result will be the same.

"It takes time and a firm conviction to persuade a woman who has made up her mind to be rid of an unwanted pregnancy not to have an abortion. Not all women, can be so persuaded no matter how forcefully the facts are put before them, but facts alone will influence a woman so situated. And it is the physician's duty to present the facts whenever the need to do so arises.

"The possibility of death should be mentioned. The statistics cited at the beginning of this article prove that the possibility is by no means remote. But this should not be the main

argument. The woman could probably cite a dozen cases among her acquaintances where abortion has decidedly not been followed by death. Her friends are alive and apparently happy today. The threat of legal consequences is still more futile. The law is clear enough, but who ever heard of a woman being brought into court on the charge of abortion? Even the abortionist is almost never indicted except on rare occasions when his victim is dead.

"Mortality is not by any means the most immediate hazard of abortion. There are, however, serious, though less obvious ill effects of which one or more follow nearly every illegal operation.

"Brill, the well-known psychiatrist, states that many psychoses are precipitated by abortion. Of 537 patients interviewed by one of us from one to three months after an abortion one third stated that they felt 'blue', depressed or overcome by a sense of guilt because of the step they had taken. The cancerophobia of middle life can often be traced to an early abortion, particularly if it has been followed by sterility. Marriage counselors find that marital disharmony is a frequent consequence, each of the partners blaming the other for the step which at the time both were agreed upon. But mental sequellas are vague, intangible, and difficult to correlate. There are other more definite after effects which may give the prospective foeticide pause if they are brought to her attention.

"There are few women who can free a long serious illness or years of semi-invalidism without a qualm, yet the former is not rare and the latter is very frequent following abortion. Often the more remote ailments are not attributed by the patient or her physician to their true cause. For every woman who dies following abortion there are four or five others who become serious ill. Peritonitis, septicemia, salpingitis, salpingo-oophoritis, pelvic abcesses, hemorrhage and secondary anemia are foremost among the immediate complications of induced abortion.

"In Russia at the beginning of the present regime abortion was legalized and any woman who preferred it to childbearing was entitled to have the operation performed at a public hospital. After a few years the privilege was revoked because experience showed that the effects of abortion were weakening the woman-power of the country. It was a mass experiment which demonstrated that the operation is crippling even when performed under aseptic conditions by skilled surgeons. What then must be expected when, as in this country, the operator is a disreputable lawbreaker working under conditions of secrecy and haste, whose only wish is to get his bloody work done and collect his money without being caught? This is true of the abortionist in the big cities where the Abortion Racket flourishes and where you sometimes hear reputable men who should know better speak of a "good" abortionist. The term is paradoxical. The practiced abortionist, who has a fancy suite of offices to impress the ladies who can afford to pay his exorbitant prices works with the same motives and under the same anxieties as his humble colleague, the village quack. He may and usually does keep several thousand dollars in cash handy to blind the eyes of justice, but he also has a back door open always for a hasty exit.

"Taussig, who visited Russia when the results of the experiment were becoming manifest, reports that immediate complications occurred in 10% of all cases, remote complications in 27%. Among the chronic conditions which developed in those who had had abortions were endocervicitis, endometritis, and endocrine disturbances. Forty-three percent of the women complained of menstrual disorders which had not been present prior to abortion. Hydatidiform mole and chorio-epithelioma were seen more frequently after abortion than following normal childbirth.

"Girls and young married women, while determined to be rid of an untimely pregnancy, usually look forward to having a family later when it may be more convenient. These recoil at the thought of permanent sterility. At a sterility clinic in New York 22% of 483 patients interviewed confessed to having had one or more illegal abortions in the past. In Russia 35% of those who wanted babies but were unable to conceive had been aborted earlier. These are among the most pitiful of the childless because they realize that they themselves are responsible for their fate.

"Among those who do carry out their plans 'at a more convenient time' parturition is likely to be more complicated. Placenta previa is four

times more frequent in those who have had abortions than in those who have not. Premature separation of the placenta, uterine inertia, rigid cervix, adherent placenta and postpartum hemorrhage all occur more frequently in these patients.

"Facts such as these should be soberly presented to the girl or woman who declares that she will 'get rid of it' in spite of every argument. Many can be dissuaded and she will live to love the child and thank the doctor who took the trouble to convince them that an abortion is more dangerous than having a tooth pulled, a fact of which not a few seem to be ignorant.

"If the physician can go further—help the single girl to make peace with her family, arrange for her confinement in a place where gossip can be reduced to a minimum, help the married woman to adjust herself to an attitude of acceptance, and show both that a baby is not the worst calamity that can come out of a pregnancy he will have done a fine piece of preventive medicine."

Penicillin, Historically Considered

C. E. YOUNT, M. D.
Prescott, Arizona

MANKIND is indebted to the action of certian moulds for many products useful in industry and for some foods. Until recently, the medical profession has been interested more in the moulds pathogenic to man and the lower animals. However, within the past three years it has been proven that a common mould, Penicillium Notatum, yields a substance called Penicillin possessing powerful bacteriostatic and bacteriocidal properties against certain pathogenic organisms.

I do not intend to involve you in a discussion of the fungi but for the purpose of orientation, a few pertinent facts are presented.

"The fungi form a large heterogeneous group of plants, including all those *lacking chlorophyl*, and because of this lack of chlorophyl, their life is restricted, and they are unable to decompose carbon dioxide of the atmosphere and are therefore dependent on other plants (rarely animals) for their carbonaceous food material." Jordan states that: 1. "They are forms that have lost the chlorophyl they once possessed as the result of taking up a saphrophytic or parasitic mode of life." 2. "Fungi with incompletely known life cycles are called Fungi Imperfecti. They constitute a large group artificially classified together while we await more knowledge of their life history." 3. "The spores or moulds are well-nigh ubiquitous and are usually more abundant than bacteria in ordinary air."

Aspergillus and Penicillium belong to the same genus. Many species of this group could be classified as "friendly moulds." They are industrially important on account of their hydrolysis of starch, sugars and tannins and their fermentations which produce, oxalic, citric and gallic acids; more rarely alcohol. Aspergillus oryzea which furnishes the Taka Diastase of commerce, Aspergillus Wentii used in the manufacture of soy bean sauces etc. Connoisseurs of cheese are indebted to Penicillium Roqueforti and Penicillium Cameinberti for those delicious cheeses.

As to classification of moulds, the late Professor Hans Zinsser of Harvard said, "The whole subject of the classifications of fungi is in confusion—even the identification of a species is often difficult, partly because some simple types show little that is distinctive in their structure but chiefly because their morphology varies greatly with changed environment."

In 1935, Professor W. C. Dodge, a former confrere of Zinsser, but now with St. Louis University published *Medical Mycology*, a most voluminous, comprehensive and authoritative work, yet he mentions only eight species of the mould Penicillium and did not include Penicillium Notatum which is the subject of the paper, and which now bids fair with its spectacular results to take the center of the medical stage held by the sulfa drugs.

It has been known since the early days of bacteriology that certain bacteria are capable of destroying other micro-organisms.

Reid as early as 1935 reported work on the inhibiting substance produced by Fleming's

Read before the Yavapai County Medical Society, June 24, 1943.

mould. He did not isolate it but noted some of its characteristics.

Then Dubos in 1939 isolated a highly potent substance from cultures, of a soil spore-bearing bacillus, Bacillus brevis, which was highly bacteriocidal to most gram positive organisms to which he gave the name "Gramicidin."

In the same year, Alexander Fleming, Professor of Bacteriology in the University of London, trying to secure selective cultures by applying to the surface of an ordinary culture medium a selective chemical, stated, "I first succeeded with this method with Penicillin." Here we had a bacteriostatic substance which was very potent with regard to streptococcus, pneumococcus, diphtheriod bacteria and some other organisms commonly found in the respiratory tracts." Fleming's simple description of his isolating experiment is as follows:

> Plant the mould in a streak across one side of a culture plate. The culture is allowed to grow at a suitable temperature for a suitable time, then the test bacteria are planted in sheets across the plate at right angle to the mould growth. If this is done with Penicillium Notatum, growth on ordinary nutrient agar for three days at room temperature it will be found that staphlycocci and streptococci will be inhibited for a distance of perhaps 30 mm. while B. coli, B. Typhosum or B. Pestis will grow right up to the mould."

Fleming not only suggested its use as an inhibitor in the isolation of certain types of bacteria but he also noted that the injection into animals of broth containing the substance was no more toxic than plain broth and he suggested that the substance might be a useful antiseptic for application to infected wounds.

Fleming's suggestion that this mould extraction might have medicinal qualities was quickly taken up by an able scientific group, known as the Oxford Group. H. W. Florey and E. Chain and their associates worked with this substance elaborated by the mould Penicillium Notatum and as a result of their studies were able to carry Fleming's original observations considerably further.

They devised ways of obtaining considerable yield of Penicillin and a rapid assay of its inhibiting power. From the culture medium a brown powder has been obtained which is freely soluble in water. It and its solutions are stable for a considerable time and although it is not a pure substance (later the pyrogens were removed) its anti-bacterial activity is very great. In their first report, *Lancet*, August 24, 1940, they experimented on cats, mice, and rats. The work was from the Sir William Dunn School of Pathology, Oxford.

With a grant from The Medical Research Council experiments on a large scale production were conducted and by a grant from the Rockefeller Foundation, technical assistants were provided and other expenses cared for.

RESEARCH IN WAR

At this time, England is engaged in war with a cruel adversary and her hospitals and colleges are being frequently destroyed by ruthless bombings, yet, be it said to their indomitable courage, scientific research went on. I am particularly anxious that you should visualize the setting or environment in the midst of which this work was performed so I will refresh your memory by quoting from the London Letter to the Journal of the American Medical dispatch of July 19, 1941.

"No one knew beforehand what would be the result of a concentrated and prolonged bombing of the vast population in the Thames valley, amounting to more than eight million people dependent from day to day on light, heat, power, water, sewerage and communications on the most complicated scale. The administration of London was confronted with problems hitherto unknown in all its history. Public order, public health, the maintenance of all essential services, the handling of millions of people who come in and out of London every day; shelter—not indeed from bombs, for that was beyond us—but from their blast and splinters; the removal of the dead and wounded from shattered buildings; the care of the wounded when hospitals were being ruthlessly bombed; provision for the homeless, sometimes amounting to many thousands in a single day; these things, with the welfare of great numbers of children, presented tasks which might have seemed overwhelming. Indeed, before the war plans were made to move the government and all the great controlling services from London and disperse them about the countryside. When the storm broke in September, water was cut off, railways were cut or broken, large districts were destroyed by

fire, twenty thousand people were killed and many more thousands were wounded. But there was one thing about which there was never any doubt—the courage and unconquerable grit of the Londoners. Without that, all would have failed. All the public services were carried on, and all the intricate arrangements involving the daily lives of so many millions were carried out, improvised, elaborated and perfected in the very teeth of the storm."

The work on Penicillin represents team work of the highest scientific order. The division of labor was as follows: The work was planned and started by E. Chain, Ph. D. Cambridge and H. W. Flory M. B. Adelaid, F.R.S. The chemical and biochemical part of the work was carried out by E. Chain and E. P. Abraham, D. Phil., Oxford. U. G. Heatly, Ph. D., Cambridge, devised the assay method and developed and supervised the production of Penicillin. M. A. Jennings, B. M., Oxford, and H. W. Flory have conducted the biological tests (except those especially mentioned in the text). A. D. Gardner, D. M. Oxford, F.R.C.S., has conducted the bacteriological investigations and made some special observations on the growth of the mould. C. M. Fletcher, M. B. Cambridge (Nuffield, research student) of Nuffield Department of Medicine has been in charge of the administration to man. The successful conduct of the work to its present stage (August 16, 1941) has only been made possible by the closest collaboration of all concerned. They published their exhaustive report in the *Lancet*, August 16, 1941. I will not weary you with a detailed report of the growth of this mould in commercial quantities, but I will make a few observations and refer you to the Life Magazine of May 24, 1943, excellent photographs illustrating the culture of Penicillium Notatum.

USE OF PENICILLIN

To grow enough Penicillium Notatum to yield 17.2 grams of Penicillin required to treat one case mentioned by the Oxford Group in their report at the rate of yield of 100 liters to produce 1 gram of Penicillin, it would take 1,720 liters of medium, quite an order in itself. But in this case some Penicillin was recovered from the boy's urine and was again used intravenously. In the first report of cases by the Oxford Group, "Penicillin, was given intravenously to five patients with staphylococcus and streptococcus infections and by mouth to a baby with persistent staphlococcus urinary infection. It was also applied locally to four cases of eye infection. In all of these cases a favorable therapeutic response was obtained." Now, I would like to quote briefly from the history of one of these cases—"case 5—boy aged 14½, admitted May 6, 1941. Staphlococcus septicemia with early osteomyelites following a fall six days before. Blood culture showed staphlococcus aureus. Sulfathiazole 64 grams given May 7 and 12 with very little benefit. May 17—left hip joint explored, no abscess found, joint contained sterile fluid with polymorphs in it. May 22—blood and albumin in the urine. Embolic pustules and rash. X-ray now shows osteomyelitis left femoral neck with involvement of joint and destruction of alveolar walls. Discharge from wound now contains staphlococcus aureus. June 6—patient still extremely ill, T. 101° degrees, much pain in left hip and thigh, urine still contains blood and albumin. Hemoglobin 74%, red blood cells, 4,290,000. Intravenous infusion of 500 mg. Penicillin in 540 cc. normal saline started at 45 cc. per hour, given for 90 hours during which time 3.5 grams of Penicillin was given. There were no reactions and his general condition was good. By June 10 he had lost most of the pain and tenderness. Cannula transferred to another vein and infusion at half rate, double strength Penicillin (1 gram to 500 cc.). On June 11 and 13 sudden rises in temperature without apparent cause were traced to the use of Penicillin prepared two months previously and containing pyrogenic impurities. On June 14, the cannula was transferred to another vein and Penicillin recovered from the boy's urine was used.

"There was no further rise of temperature and steady improvement. On June 16, the continuous administration was stopped. He was given another 50 mg. 3 hourly of 12 doses then 4 hourly for 12 more doses. Stopped June 20, with a total dosage of 17.2 grams. (As just stated at the rate of usual yield and not using Penicillin recovered from the patient's urine, 1720 liters of medium would have had to be extracted to recovered this amount of Penicillin.) (I note here the difference in the article in *Life* magazine published two years later which gave a yield of 10 grams of Penicillin from only 160 liters of medium.) On June 23

X-rays showed no extension of destructive processes, the urine was normal at that time. On July 11 the patient had been afebrile for 3½ weeks, with no pain in the leg. The white blood cell count were as follows: June 6, 9400; June 13, 9400; June 14, 16,000; June 21, 12,400. This was a case of Staphlococcus Septicaemia, localized in the left hip joint, which had been uninfluenced by large doses of Sulfathiazole in the early stages. When Penicillin was started the patient was extremely ill, in great pain and had an acute nephritis. There was striking improvement in the general condition during the period of therapy. All the pain in the region of the left hip disappeared and the nephritis was clear and the temperature was normal."

Another case, No. eight, was that of a girl, 19 years of age who had burned her face with a cigarette end six weeks before admission. The burn became infected and from this a septic rash spread over the face. A week before her admission the left eye became red, swollen and painful.

On admission, June 9, 1941, there were many small crushed impetigo-like spots on both sides of the face. The left conjunctiva was inflamed and showed a thick mesh of fine vessels, the cornea clear, and the eyelids slightly swollen. The eye bath was filled with 1-2500 Penicillin. The next day there was less infection and the eye was not painful. After three days, the eyes were almost normal; the treatment continued with drops 1-500 Penicillin, 2 hourly by day and 4 hourly by night. On June 13, the eyes were completely normal, on and after June 10 an ointment consisting of 1-500 Penicillin in hydrated lanolin was applied to the rash on the face twice daily. When the patient was discharged on June 15, the eye had healed completely with only slight residual erythema.

AMERICAN RESEARCH

Now let us see what we in the United States have been doing with Penicillin. Experimentation has been going on in the United States with Penicillin. Charles H. Rammelkamp and Chester Keefer from the Evans Memorial, Boston University School of Medicine, reported in the *Medical Record* (received for publication December 7, 1942) "No Penicillin was found in the spinal fluid, saliva, or tears in subjects receiving it intravenously. In the presence of renal failure Penicillin was not excreted rapidly and as a result high concentrations were maintained in the blood stream."

Mayo Clinic: They received Penicillin early. Dorothy H. Heilman, assistant, Division of Experimental Surgery and Pathology and W. E. Herrell, Division of Medicine, reported on "The Comparative Anti-Bacterial Activity of Penicillin and Gramicidin: Tissue Culture studies." Reporting on May 27, 1942, they concluded:

(1)—Purified gramicidin and a highly concentrated (1-200,000) preparation of Penicillin have been found to be of the same order of activity against strains of gram positive cocci.

(2)—There are well marked differences in the selective bacteriocidal activity of these two substances.

(3)—Penicillin and gramicidin act on bacteria at a slow rate.

(4)—Although small amounts of Penicillin and gramicidin may be only bacteriostatic, there is evidence that both substances may be bacteriocidal under certain conditions.

(5)—Neither of these substances enhances or inhibits the bacteriocidal action of the other.

W. E. Herrell recorded "Further Observation on the Clinical Use of Penicillin," May 10, 1943. Among other things he states, "Fortunately, Penicillin, unlike many similar substances has been found to be relatively non-toxic and at the same time bactericidal under certain conditions. It is my opinion that the continuous intravenous administration of pyrogen-free Penicillin is the most suitable method of treating severe infections of staphlococcus aureus, streptococcus pyrogenes, susceptible strains of Diplococcus pneumoniae, Neisseria Gonorrhea and Neisseria intracelularis. On the basis of experimental evidence it should prove useful in the treatment of infections associated with gas gangrene. Because of its activity against actinomyces bovis, clinical trials are now being undertaken. It is my opinion that the continuous or nearly continuous intravenous administration of pyrogen free Penicillin is the most suitable method of treating severe infections of the type considered previously. The material rapidly disappears from the blood stream into the surrounding tissues and is rather rapidly

excreted in the urine. Periodic intravenous injections of relatively large amounts of Penicillin followed by an interval during which the amount of material in the blood is almost negligible may do much to encourage the development of so-called Penicillin-resistant or Penicillin-fast pathogens."

His concluding remarks are as follows, "To insure the best results in using Penicillin, care must be taken in the selection of the type of care for treatment. Only through the selection of infections attributable to organisms susceptible to Penicillin can unfavorable results be presented."

Herrell's case 5 is reported in detail and the photographs taken, graphically illustrate a wonderful cure for, "an infection of this type complicated by septicemia is almost universally fatal." (Staff meeting of the Mayo Clinic, March 10, 1943, p. 65.)

Mayo Clinic (May 29, 1943): The most recent report from the Mayo Clinic appeared in the *J.A.M.A.* of that date with W. E. Herrell as co-author with E. N. Cook, M. D. and Luther Thompson, M. D. entitled "The Use of Penicillin in Sulfanilamide Resistant Gonorrheal Infections." The Abbott Laboratories, Incorporated prepared the Penicillin used, though they, the Mayo Clinic, have prepared small amounts. Their summary is as follows: "When studied experimentally the anti bacterial activity of Penicillin against several strains of Neisseria Gonorrhea isolated from patients in whom the infection was completely resistant to what might be considered adequate treatment with sulfanilamide preparations. These strains of organisms are inhibited completely in fairly high dilutions of an active form of Penicillin. Bacterial cultures reveal that the number of organisms is decreased greatly at the end of one or two hours contact with Penicillin. Between the second and third and fourth hours in contact with Penicillin, no viable organisms were found. The complete absence of toxicity following the intravenous administration of Pyrogen free Penicillin, the lack of any discomfort to the patient and the rather rapid disappearance of clinical symptoms have been observed in three cases of sulfanilamide resistant gonorrheal infections. Because of the limited amount of Penicillin available, we feel that Penicillin therapy should be reserved and studied further in those cases in which the infection is resistant to the accepted forms of treatment now being used.

In all the cases reported, in addition to the clinical response noted, negative bacterial cultures were obtained sometime between 17 and 48 hours after the institution of Penicillin Therapy."

"Intensive study of the process of cultivation of this mould by scientists in Governmental Universities and commercial laboratories is resulting in the production of increasing amounts, so that the scope of its use in human disease is being rapidly extended," says A. R. Dochez, M. D.

I wrote to Merck and Co. and to the Lederle Laboratories, Inc. and also to the Surgeon at the Bushnell General Hospital at Brigham City, Utah. They were all kind enough to reply. I will quote in part from their letters.

A. From the Lederle Laboratories:

"While our laboratories are conducting some experimental studies on Penicillin at present none of the material is available for distribution.

"Whether production should be concentrated on the natural or synthetic is still a moot point. Synthetic means, if possible, would increase the supply.

"Our laboratory, however, is preparing a review on the subject of Penicillin and we will be glad to send you a copy as soon as this becomes available."

B. From Merck & Co., Inc.:

"As to the work that has been done with it in the past year, all of the investigations have been under the exclusive control of the Committee on Chemotherapy of the Office of Scientific Research and Development. A brief summary of the results of these studies was presented by Dr. A. N. Richards, Chairman of the Committee on Medical Research, in the May 22nd, 1943, issue of the *Journal of the American Medical Association*, page 235. We are not at liberty to disclose any information beyond what he has presented. It is possible, however, that if you address him directly at the University of Pennsylvania Medical School, some further data might be released.

"As to the question in the second paragraph of your letter, we can only say that the synthesis of Penicillin has not yet been accomplished, although some progress in that direction is being made. We are currently producing appreciable

quantities of it by cultivating the mould, *Penicillium notatum.*

All of this material at the present time, however, is being required by our armed forces."

C. From the Bushnell General Hospital:

(Henry G. Hollenberg, Lt. Col. Med. Corps, Chief of Surgical Service).

"I can only say at present that we have been using it both intravenously and locally and are enthusiastic about it. We have found it to be quite efficacious in the treatment of severe infections, both local and generalized when caused by any of the coccus family and in some cases when caused by b. coli. It is ineffective against b. proteus and b. pyocyaneus. It has been particularly effective in cases of chronic gonorrheal urethritis and in the only two cases of streptococcus bacteremia which we have had, we have gotten negative blood cultures in twenty-four hours. We have not had the opportunity to explore its usefulness in all of the various infections for which it is reputed to be effective but we are gradually getting together a large number of cases."

In conclusion, I would not venture a prediction on the future place of Penicillin in Medicine and surgery but from the data presented you must agree with me that it is a "child of great promise" and merits further scientific study by our universities, government and "Private grants in aid" and our large commercial houses; all of which is being done.

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Early Treatment of Compound Fractures

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IN the first World War we were greatly impressed by several new principles of treatment that materially reduced morbidity and mortality in the fighting forces. When one recollects that in the Civil War and the Spanish-American War more deaths were due to typhoid fever than to battle casualties, one appreciates the miraculous reduction of the disease that resulted from the routine administration of typhoid and paratyphoid prophylaxis. In the cases of the wounded, prevention again played a distinct role. The regular use of antitetanic serum and antigasbacillus serum undoubtedly saved many lives. The development of the Carrel-Dakin treatment in compound wounds was outstanding in the early cleansing of wounds, the elimination of fever, and the reduction in the amount of surgical dressings necessary, even though its proper technique did involve exact concentration of the hypochlorite solution, proper temperature to prevent evaporation, and a constant irrigation of the deep wounds with very careful daily dressings. The principle of prompt splinting of fractures of the long bones served to prevent much shock, not to mention the relief of much suffering. And at the end of the war the now famous Orr treatment of early debridement, thorough packing of the wounds with vaselinized gauze, and the application of plaster casts with absolute elimination of daily dressings proved to be another step forward in the successful treatment of severe wounds.

Read before the New Mexico Medical Society Annual Meeting, Santa Fe, June 26, 1942.

NEW TREATMENT OF WOUNDS

And now another epoch-making chapter has been written in the treatment of severe wounds, especially those associated with contaminated compound fractures. This new treatment is indicated not only in fresh wounds, but also in old infected wounds where further operation is necessary to correct malunion or non-union or to heal persistently draining sinuses. And in instances of apparently clean wounds where later infection is feared, this new treatment can

be counted on in most cases as a more or less sure method of prophylaxis. I refer to chemotherapy with the sulfonamide group, particularly sulfanilamide and sulfathiazole.

In 1908 a German chemist by the name of Gelmo, while studying azo dyes, was the first to mention sulfanilamide. Five years later Eisenberg noticed the bactericidal powers of some of the azo dyes and suggested they might be used practically. In 1932 sulfanamidochrysodine was patented as prontosil. Soon it was found to be specific in overcoming streptococcic septicaemia in mice, and by 1935 it was first used clinically. In the United States prontosil was probably first used in June 1936 on a patient with acute mastoiditis and lateral sinus thrombosis. The first publicity in our American Journals was given in an article by Long and Bliss of Johns Hopkins in January, 1937, reciting certain confirmatory observations of numerous European investigators that para-amino-benzene-sulfonamide exerted specific chemo-therapeutic effects in Beta hemolytic streptococcic infections and advising that careful clinical use of this drug and its derivatives was warranted in treatment of Beta hemolytic streptococcic disease in human beings. This drug was found to be also very effective against gas forming anaerobic organisms, particularly the Welch bacillus.

An article by Jensen, Johnsrud, and Nelson appearing in Surgery in July, 1939, was the first to give a complete report on the local implantation of sulfanilamide in compound fractures. These writers gave a resume of the history of the treatment of compound wounds by surgical excision of devitalized and contaminated tissues from traumatic wounds dating from Petit in the early 18th century. Much hospital gangrene had occurred. Lister in 1867 treated compound wounds with carbolic acid packs, but this antiseptic agent was harder on the normal tissue than on the infected areas. Such continued to be the case with all antiseptics with the exception of Dakin's neutral hypochlorite of soda. And now that Long and Bliss had just revealed two years previously the effective principle of prontosil to be sulfanilamide, and demonstrated its bacteriostatic properties in dilutions of 1-10,000, these writers first experimented on a boy of twelve years with compound fractures of both bones of one leg in addition to multiple other injuries and severe shock. After careful and thorough debridement and local implantation of five grams of sulfanilamide following shock therapy the boy recovered. After that thirty-nine compound fractures were so treated, without a single case of infection, although previous to this sulfanilamide treatment infection had occurred in compound fractures at the Minneapolis General Hospital in 27 per cent of their cases over a period of years. After this remarkable and almost unbelievable communication, reports have flooded literature as surgeons have given particular attention to this chemotherapy. Of course, chemotherapy per se is not new when one considers the use of tobacco, Chinese herbs and various poultices faithfully applied to wounds of battle or of peace. These were gradually discarded for carbolic acid or even Dakin's solution, all applied from the outside. As systemic agents we are still using the various protective sera for tetanus, gas gangrene, and the specific drugs for malaria, syphilis and the like. But this new chemotherapy is really new and different. The sulfaonamide drugs are given both systemically and locally from within the wound, not from without.

But sulfanilamide and its derivatives must not be considered bactericidal. They do not kill the bacteria but inhibit their growth and are therefore bacteriostatic in therapeutic doses, though possibly bactericidal in excessive doses. While they therefore prevent the growth of bacteria, the job of killing the organisms rests with the resistance of the individual by the development of antibodies. When given by mouth the effectiveness depends upon the concentration of the drug in the blood. This concentration is limited in therapeutic doses to 20 milligrams per cent, but when given locally the concentration at the site of the local wound may be forty times as great. While it is true that sulfanilamide in the blood stream is rapidly distributed to all the soft tissues, bone tissue is reached more slowly because here the water concentration is much less. Hence the indication for local application of the drug. Key of St. Louis is the man who has emphasized more than anyone else the extreme advantage of local administration. He has done much experimentation along this line and has proved conclusively that while the primary healing seems occasion-

ally slower, that the ultimate healing is in no way retarded. He has proved that the administration of sulfanilamide directly into the tendon sheaths and into the joints has had no ill effects. He also proved that not only is the concentration forty times as great when the wound is tightly closed, but that effects persist for a much longer period of time.

As to the choice of the particular sulfonamide, sulfanilamide has proved much more popular than sulfathiazole, or sulfapyridine or sulfadiazine in compound fractures. Theoretically, sulfanilamide is specific for certain strains of hemolytic streptococci, and to a less extent favored for staphylococci and the gas bacillus of Welch, while sulfathiazole is supposed to be more useful in combating gonococci, pneumococci, staphylococci, and the Welch bacillus. Sulfapyridine is also indicated in these four latter organisms, but is only one-third as soluble as sulfathiazole, while sulfathiazole is only one-tenth as soluble as sulfanilamide. A frequent combination is the use of sulfanilamide locally along with the oral use of sulfathiazole. Though sulfanilamide was the first and most popular drug, I believe there is a general tendency now to using more and more sulfathiazole in its place.

There are, of course, certain toxic manifestations that may arise with the administration of the sulfonamides. And some individuals may show some unpleasant complications with one derivative but not with another. Cyanosis not infrequently occurs, but is not an indication for discontinuing therapy. Some patients complain of nausea, vomiting, and diarrhoea, especially after a large initial dose. These symptoms are not serious and can usually be governed by decreasing the dosage, or substituting a different derivative. The same applies in complications of headache or dizziness. A fairly frequent finding is a temporary mental aberration, which will easily clear up on cessation of the drug. Acidosis is usually controlled by soda bicarbonate given in equal parts. If this is not sufficient, the drug must be stopped. An unusual complication in this therapy is a febrile reaction or so-called drug fever. It may occur after the drug has been given for five to ten days, and after the patient is showing clinical improvement, and may be accompanied by other toxic reactions of chills, tachycardia, and vomiting, and may rise to 104° or 105°. Because of this hypersensitivity, it is well to question patients about previous experiences with the drug. Treatment, of course, is to discontinue the drug and push fluids. Skin eruptions may occur which simulate measles or scarlet and many other types of rash. Occasionally a hemorrhagic eruption is found. Sometimes a red nodular lesion appears, accompanied by erythema of the buccal mucous membranes. Conjunctivitis, scleritis and painful joints show up sometimes. Usually the drug therapy should be stopped when these phenomena occur, but first of all another sulfonamide may be tried. A dermatologist should be consulted. Jaundice from liver damage must be mentioned. In fact, some writers believe that a majority of patients with severe infections show clinical or laboratory evidence of liver dysfunction. Sulfathiazole causes less liver damage than sulfanilamide. If hepatitis is recognized, therapy should be discontinued, and a high carbohydrate diet advised. Another complication to be looked for is anemia which may show up within a few days; it is seen more frequently in children than in adults, is more likely to occur with sulfanilamide than with sulfathiazole. Transfusion may be indicated in the severe cases. If the anemia is an acute hemolytic type, the drug must be stopped at once. Leukopenia occurs much less frequently than anemia, but certainly should be watched for by frequent blood counts. It does not occur until the drug has been given a long time. The most serious complication is malignant neutropenia terminating in fatal agranulocytosis. To prevent this chemotherapy must be stopped if the white count falls below 4,000. Complications of the urinary tract bear watching; it is very seldom that damage occurs when sulfanilamide is used, though more often with sulfathiazole, probably because of the low solubility of the latter. Look for a diminished output or hematuria or rise in nonprotein nitrogen content of the blood. If the hematuria is only microscopic, probably chemotherapy need not be stopped. The urinary output should be maintained at 1000 cc. for twenty-four hours. The appearance of sulfapyridine or sulfathiazole crystals in the urine is frequently encountered, but is not sufficient indication for stopping the drug, although precaution must be exercised. The use of alkalines has apparent-

ly very little bearing in the prevention of urinary tract complications.

And now the indications: While this chemotherapy is primarily designed for fresh badly contaminated wounds with or without compound fractures, there have been added three other conditions where sulfonamide therapy is distinctly indicated. First we have the chronic wounds where there is continued failure of closure or persistence of draining sinuses due to retention of devitalized tissue or chronic infection such as osteomyelitis with sequestration. Secondly, we may use the drug in previously infected but healed wounds where further surgery is necessary as in instances of malunion or persistent non-union; these may be considered potentially infected wounds. And lastly it is used in fresh surgical wounds especially where on account of extensive operative procedure, or considerable exposure of bone and soft tissue, prophylaxis is desirable. Key of St. Louis has proved without dispute that the incidence of infection in clean wounds where the sulfonamides are used as prophylaxis is very much less than where the group is not used. This is particularly true where internal fixation is used. The healing of clean wounds is not hampered by the implantation of sulfanilamide or sulfathiazole, as shown clinically and as proved by much experimental work, particularly on rabbits.

What are the advantages of chemotherapy? The answer may be briefly summarized as follows: If properly carried out, the advantages include primarily prevention or decrease of infection and consequently earlier healing, and what is just as important, the use of the sulfonamides allows the immediate reduction of fractures, the application of internal fixation thus preventing shortening, malunion, and in the vast majority of cases non-union.

COMPOUND FRACTURES

But let us not be so enthusiastic about the sulfonamide treatment that we lose sight of certain underlying principles in the treatment of compound fractures that have come down to us from the ages. First of all, let us bear carefully in mind that the local and oral use of these drugs does not excuse us from carrying out at the same time such procedures as will enable the sulfanilamide to do its essential work. The thorough cleansing and debridement of wounds is after all even more important than the simple implantation of sulfanilamide. This chemotherapy will fall into disrepute if we in the least neglect other essential methods of treatment. Sulfanilamide and is derivatives are not all powerful by any means. Many operations in bygone days have been discredited because they are not carried out to the letter or followed out after the manner of their authors. Thorough, painstaking cleaning of the skin about the wound, exacting debridement of the whole wound, and copious irrigation are absolutely necessary. Proper splinting and proper fixation are essential. Good closure is paramount, and the administration of sera is not to be neglected.

The technique of chemotherapy in fresh compound fractures has become more or less standardized. The routine may vary a little with the surgeon and with the individual case, but certain definite principles are adhered to. If the wounded man is seen at the place of injury, first-aid demands the application of a sterile dressing, possibly a tourniquet, and if convenient a dash of sulfathiazole powder over the lacerated area. A temporary transportation splint should be applied, especially if the lower extremity is involved, after the man has been given a sedative. The most practical splint is the well known Thomas leg or arm splint. As described in the First Aid text book, there are two convenient modifications for practical use, the Keller-Blake hinged half-ring splint for the leg or the Murray Jones hinged arm splint for the upper extremity. The advantages of immediate splinting, of course, are the prevention of shock and the alleviation of pain, as well as the reduction of further damage to the bone or soft tissue. After the man has been brought to the hospital the first treatment is essentially shock therapy, and here again we may give some sedative, preferably morphine, and apply some form of traction if the long bones are involved. In severe cases transfusions of whole blood or blood plasma may be utilized, together with measures to keep the individual comfortably warm, but not too warm least excessive perspiration depletes the salt content of the blood, a very important consideration as recently brought out. After the person is out of shock or apparently well on the road to recovery, he should be taken to the operating room and prepared for operation under general

anaesthetic of cyclopropane or pentathol sodium. Some surgeons advise the immediate placing of the lower extremity in the traction apparatus if the femur or tibia is badly fractured as disclosed by X-ray. Then the skin about the wound is thoroughly cleansed with warm water and green soap and shaved, and is rendered aseptic by alcohol, ether, and merthiolate or mercresin. The wound is flushed with warm saline and perhaps scrubbed before draping the leg and beginning the debridement. A tourniquet is usually applied. After this the painstaking process of debridement is begun, going from without inward. The skin edges are carefully cut away to remove any necrotic or traumatized portions. The contaminated fascia is carefully trimmed. All foreign matter is removed. Torn muscle is either discarded or sutured where indicated, careful hemostasis is performed as every corner of the wound is exposed and inspected. The bone fragments are exposed, and scrupulously cleansed, removing by the rongeur any dirty bone ends. After such thorough toilet, irrigation with warm saline follows, using perhaps as much as 5 liters, and then again removing any more devitalized tissue thus brought to light. The fragments of bone are now brought into alignment, and the fracture reduced. If internal fixation is deemed necessary, we insist on vitallium or stainless steel which has been proved to show no electrolytic action on the tissues. A Lane plate or Parhamband is applied depending upon whether the fracture is transverse or oblique. As a rule we do not countenance the use of wires for internal fixation, though we thoroughly approve of Kirschner wires or Steinman pins for external fixation. After the fracture is set the implanation of sulfanilamide crystals or sulfathiazole powder is made by placing the drug in absolutely every corner of the wound, using usually 5 to 15 grams, with a maximum limit of 20 grams. The wound is now securely closed, after thorough hemostasis. As far as possible deep sutures are avoided, but the skin and subcutaneous tissues are closed securely without any drain whatsoever since such a procedure would allow serum to leak out and thus spoil the high concentration of the sulfonamide drug. Proper splinting is now applied, whether it be a small wooden or metallic splint or a firmly fitting plaster cast. Before the patient comes out of the anaesthetic, he is given the antitetanic serum and the antigas serum, though some surgeons are now omitting the latter on the ground that the sulfonamides, particularly sulfathiazole are specific against the Welch bacillus. In addition to the local implantation of the drug, we begin the next day the oral administration. A heavy initial dose of sulfathiazole, often 90 to 120 grains, is given each day for three days, then the intake is cut down to 45 grains a day for the next week. We watched the blood count for signs of any anemia or leukopenia, and insist on a sulfanilamide concentration test, lest there be more than 15 milligrams per cent. Such is our procedure in fresh compound fractures. The only deviation from this routine is in cases of very extensive wounds which we have not dared to close in their entirety or where not sufficient skin is present to effect a closure. Here we utilize in part the Orr treatment, using vaseline strips to cover the exposed areas. And the routine as described cannot be followed if operation is not done within twelve to fifteen hours.

CHEMOTHERAPY IN OLD WOUNDS

As mentioned earlier, the fresh severe wounds with contaminated compound fractures are not the only indications for this chemotherapy. Many chronic wounds with persistent drainage from devitalized areas, whether it be soft tissue or sequestrating bone, offer opportunity for chemotherapy. Such a wound may be opened up widely, the offending sequestrum removed, implantation made and secondary closure done. Remarkable results frequently follow. Then in instances of non-union or malunion where there has been no discharge or other evidence of infection for many months, sulfanilamide comes to our rescue. It has been the experience of many surgeons that such wounds, when opened up again after months of quietude, will flare up on surgical interference, even when no evidence of faulty technique can be discovered. This potential infection seems to lurk for years. In such cases as this when it is decided to go into an old wound to correct a malunion or to overcome a non-union, sulfanilamide is given for two to three weeks preceding the operation in relatively small doses of about three or four grams a day, with a larger dose just before surgery. The fourth indication for sulfonamide therapy is that of prophylaxis. Key of St.

Louis was the first to make a thorough study of this phase, and on the hypothesis that every operative incision is potentially an infected wound, he now routinely implants sulfanilamide in all his clean operative wounds before the wound is sutured. He reports that in over 150 consecutive wounds, no post-operative infection developed. He does insist that the drug should be sterilized by autoclaving at fifteen pounds pressure for thirty minutes.

The efficacy of chemotherapy with the sulfonamides was borne out recently by their use at Pearl Harbor on last December 7. The reports given in a recent Army Medical Bulletin relate in detail how the various injuries were sorted as to the necessity for immediate treatment, how crystalline sulfanilamide was placed in the wounds which would have to wait for a time. The abdominal and chest wounds had to be attended to first, and these received ample chemotherapy. The compound fractures were treated by debridement, and implantation of sulfanilamide, though no internal fixation or closure was done, but external fixation used. It was the practice not to dress open wounds frequently, but when they were dressed, further application of sulfanilamide were given, and sulfathiazole or sulfadiazine by mouth, a dosage of four to six grams of drug per day for seven to ten days after operation. Ether was preferable to spinal anaesthesia or pentathol sodium by vein. Generous quantities of morphine, and blood plasma were used. Later examination of the wounded at Letterman General Hospital in San Francisco proved the great value of the sulfonamide drugs.

CONCLUSIONS

1. Chemotherapy by the sulfonamide group in freshly lacerated wounds with compound fractures, when combined with thorough debridement, copious irrigation, internal fixation, and immediate closure has proven a marked improvement over previous measures in reducing post-operative infection.

2. Immediate internal splinting makes for earlier union in fractures, better alignment and elimination of shortening.

3. The drug does not injure normal tissue, and does not interfere with ultimate healing when given locally.

4. Oral administration should go hand in hand with local implantation. The latter method provides a local concentration which is 40 to 80 times as great as the blood concentration provided by oral administration.

5. The drug may be used as prophylaxis in clean wounds, or in old healed wounds where further surgery is necessary.

6. The drug is not bactericidal but rather bacteriostatis, inhibiting the growth of staphylococcus, streptococcus, pneumococcus, gonococcus, and gas forming bacteria.

7. Sulfanilamide is probably preferable in most cases to sulfathiazole, principally because of its greater solubility.

8. For internal fixation, vitallium and stainless steel are the preferable metals because non-electrolytic, and hence non-irritating.

9. Toxic symptoms must be watched for. Blood must be examined frequently for anemia and leukopenia. Sulfanilamide concentration must be observed frequently. 10 to 15 milligrams per cent is the optimum concentration.

10. The drug is not a panacea, but certainly is the best we have to offer at the present time.

Results of Thoracoplasty*

(A Five and Ten Year Review)

VICTOR STRONG RANDOLPH, M. D.
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I have always felt that the evaluation of results of surgery in the tuberculous, particularly thoracoplasty, should be made after a period of time, because improvement in this disease may often be temporary. Then, since we are interested in cure, I believe that restoration of the patient to social and economic life is the final test of what has been accomplished.

In 1937, before this association, I analyzed the results of thoracoplasty in persons who had been operated upon five years or more before. Only twenty-four cases were then considered. We found that about 65% were arrested or definitely improved. 33 1/3% were restored to

* Read before Arizona State Medical Association: Tucson, April 30-May 1, 1943.

active life. 33 1/3% were dead of tuberculosis.

Of these, now 37.5% are at work or able to work, 53.7% are dead, one case is improved. One man is living, but has disease in the contralateral lung.

Three years later, at the Chicago meeting of the American College of Surgeons, I again reviewed the five-year cases which numbered seventy and it was found that 42.8% were at work or able to work, 41.4% were dead.

Reviewing now the patients operated upon five years or more ago, we find one hundred twenty-five. Of these fifty-four or 43.2% are dead, sixty-eight or 54.4% are arrested or improved and fifty-two or 41.6% are at work or able to work. Three patients are alive but unimproved.

In the ten-year group, those operated upon ten years or more ago there are thirty-two. Of these, thirteen or 40% are at work or able to work, fifteen or 46.5% are arrested or improved and seventeen or 53.1% are dead. One is unimproved.

As time goes on, we should find the results of thoracoplasty better, for some improvements in the operation, in the anesthetic and in the pre-operative and post-operative care will still occur; but particularly, we will find the general knowledge of this type of surgery widening, and patients will be submitting to it earlier in their disease when the opportunities of success are greater. Even as late as thirteen years ago, the majority of persons operated upon had extensive tuberculosis in one lung so that a total thoracoplasty was necessary. Then we began to see patients who had only a part of one lung involved and who could be cured by a partial operation. This is now the general rule. We have reached a point in public knowledge when people seek the operation.

TECHNIQUE

Our technique has changed. You may remember that fifteen years ago, the total thoracoplasty of Sauerbruck was the procedure of choice. This was done in two stages, five ribs being cut at the first operation and six ribs at the second, or vice versa. This was a very shocking procedure and was used in most of my first twenty-four cases. We then found that less should be done at one time. Later we found that longer sections of rib should be removed over certain large cavities and then that the transverse processes of the spine should be removed in treatment of cavities which reached close to the mediastinum.

About three years ago the Semb procedure was introduced in this country. This is an apicolysis or freeing of the lung at the apex and along the upper mediastinum which does give a better collapse of large apical cavities. However, it is not without danger and should be used carefully. Preliminary lysis of the lung and extra pleural pack with paraffin or some other substance has been used by some surgeons, but is not in general vogue.

The original operations of Sauerbruck were spaced from ten days to two weeks apart. We found that we could wait longer, even several weeks, giving the patient time to recover from one operation before doing the next.

ANESTHESIA

In the matter of anesthesia, we have perhaps made some progress. Some men have used, and I believe still use, certain mixtures of ether. I have always avoided this and it is not in general use. My early work was all done with local anesthetic or with ethylene. (I still consider local anesthetic the safest.) I recently performed successfully two stages of thoracoplasty, resection of five large rib segments including the entire first rib for a sixty-two year old woman under local anesthetic. I felt that any general anesthetic would have been more shocking.

Then from ethylene we went to cyclopropane. This, I believe, is a very valuable anesthetic, superior to ethylene in that more oxygen may be used with it. Archibald, the pioneer of thoracoplasties in the Americas, used nitrous oxide for many years. This may be of value when carefully used. However, in one case of mine this was used for induction. No additional anaesthetic was needed during the operation, although I did not know this at the time. The patient died apparently of nitrous oxide changes in the brain. So I have since avoided this anesthetic. But for some time now, in many cases I have been using sodium pentothal with or without oxygen. This has as its principal advantage that the anesthetist need not have the careful technical training which is essential for ethylene or cyclopropane. It has the advantage for the patient that it avoids the greater or less agitation which accompanies induc-

tion with an inhalation anesthetic. So far I have seen no ill affects.

SELECTION OF CASES

More important probably than the type of operation or the anesthetic is the selection of cases. In my work, unfortunately, I cannot say that selection has always been possible. No case that offered any hope of success, however small, has been refused. But the preliminary care has usually been dictated and the time of operation selected when possible. In general, thoracoplasty should be given only to the good "chronic case of Brown." This means a patient should have had long months of bed rest in preparation. It is desirable that the acute stages be overcome. However, I have operated sucessfully at times on patients who could not become afebrile—one, I remember, who had persistent daily temperature to 102°.

The contralateral lung should be good. Occasionally one must operate on a patient who has a questionable area in the better lung, and often these will clear up later. I have operated upon two patients I remember who had persistent scattered rales in the opposite lung but whose x-rays did not show localized exudative lesions. Their rales disappeared after surgery.

Frequently I have asked the internist referring a case to give pneumothorax in the contralateral chest before resorting to surgery on the badly diseased side. In a number of these cases, thoracoplasty has been successful a year or more later.

I think we must emphasize that in this work each patient must be very carefully studied, and that every possible advantage must be given to him or her before we undertake what is after all a serious procedure and one which will probably spell life or death.

CARE OF PATIENT

Of post-operative care I have learned a great deal. There are some very important items. First, the blood pressure must come back to normal after surgery. Do not depend on drugs, although occasionally ephedrine may be needed for quick restoration. But the most effective method is to give fluids freely and intravenously. In the majority of patients, but not all, transfusion is of value. The blood pressure must be maintained steadily from twelve to twenty hours. I remember well a patient of years ago whose blood pressure was not maintained because of a nursing neglect. When I saw him twelve hours after surgery, it could not be restored and he died.

Second, the patient must cough and expectorate as freely as possible, even though it hurts. This avoids atelectasis which can occur easily in these cases. In the third place, the patient must move his arm on the operated side from the start. Failure to do so may result in stiffness of the joint. Full motion of the arm should be restored.

Fever is to be expected on the second and third days after surgery. If it persists, something is wrong. I have found the sulfonamide drugs of some value in combating infections at this stage. Rarely the fever may be due to pleural effusion and is not readily controlled quickly. In one week's time normally the patient should be fully convalescent.

Then there should be a long period of bed rest. The thoracoplasty will have compressed the diseased lung, but this still needs time to heal. The period of time necessary is, in my opinion, at least six months, but many surgeons dictate a time of one year or more before allowing the patient to move about.

In the old days phrenic paralysis was often practised as a preliminary to thoracoplasty and was of value in those old cases where the whole of one lung was affected. Today, I think it is usually not of value. The average case has disease of the upper lung which can be controlled only by thoracoplasty. Such cases have need of their diaphragms after surgery has been performed. Several of my patients who have had successful upper thoracoplasty would be infinitely better today had some one not previously paralyzed the diaghragm permanently on the operated side.

COMMENT

I keep hoping we shall show better results from thoracoplasty, and perhaps we will. At least, in one hundred and one cases operated upon in the past five years, I have had four deaths in about two hundred and fifty operations. One of these deaths already mentioned I felt was due to the anesthetic. In other words, the operative mortality has been reduced to less than 2%. What the end result in these patients may be will be determined by the nature of their disease and the degree of control that has been exerted by their surgery.

AMERICA AT WAR

DEFENSE AMBULANCES

Plans have been announced for distribution of 800 four-stretcher ambulance bodies to cities in target areas.

These ambulance bodies, when mounted on the chassis of used passenger cars to be provided by the city, will represent a major step in strengthening the Civilian Defense measures of American cities.

Designed after extensive study, the OCD ambulance body is made of wood and non-critical materials. It can be mounted on the rear portion of the chassis of a Ford, Chevrolet or Plymouth four-door sedan, models 1939-41, after the part of the body behind the front seat has been removed.

The ambulances are roomy enough to carry four stretchers on built-in racks and still leave space behind the stretcher rows for an attendant to ride with the casualties and give necessary care enroute. The body has been approved by the Corps of Engineers of the Army.

The ambulance bodies will be distributed free of charge by OCD to selected communities, but because of the limited number available, will be sent only to cities in exposed areas—and then only after the city has notified OCD that the chassis on which to mount them will be furnished.

CIVIL SERVICE FOR DOCTORS

The critical shortage of physicians to engage in vital war work in the civilian branches of the Government continues. The great need for these men resulted in the announcing of a liberalized civil-service examination for Medical Officers in 1941. The Civil Service Commission has just revised and re-announced this examination.

The twenty optional branches under which doctors may apply range from General Practice to Aviation Medicine. Those appointed will perform professional duties as doctors of medicine in active practice in hospitals, in dispensaries, or in the field or in rural areas; or in bureaus of the Government such as the Veterans Administration, Civil Aeronautics Administration, Public Health Service, and Food and Drug Administration. Doctors will also be used in industrial establishments under direction of the War Department.

Applicants for all grades must have received the degree of M. D. from an accredited medical school. Applicants for the Senior Medical Officer grade ($5,228 a year) must have had at least 5 years of appropriate medical experience; for the Medical Officer grade ($4,428 a year), 3 years of experience in addition to a required interneship; and for the Associate Medical Officer grade ($3,828) 1 year of interneship. The salaries quoted include overtime pay.

There are no written tests and no age limits. Persons now using their highest skills in war work should not apply for these positions. Appointments in Federal positions are made in accordance with War Manpower policies and employment stabilization plans. Before a definite offer of appointment is made, eligibles are cleared through the Procurement and assignment Service for Physicians, Dentists, and Veterinarians, of the War Manpower Commission.

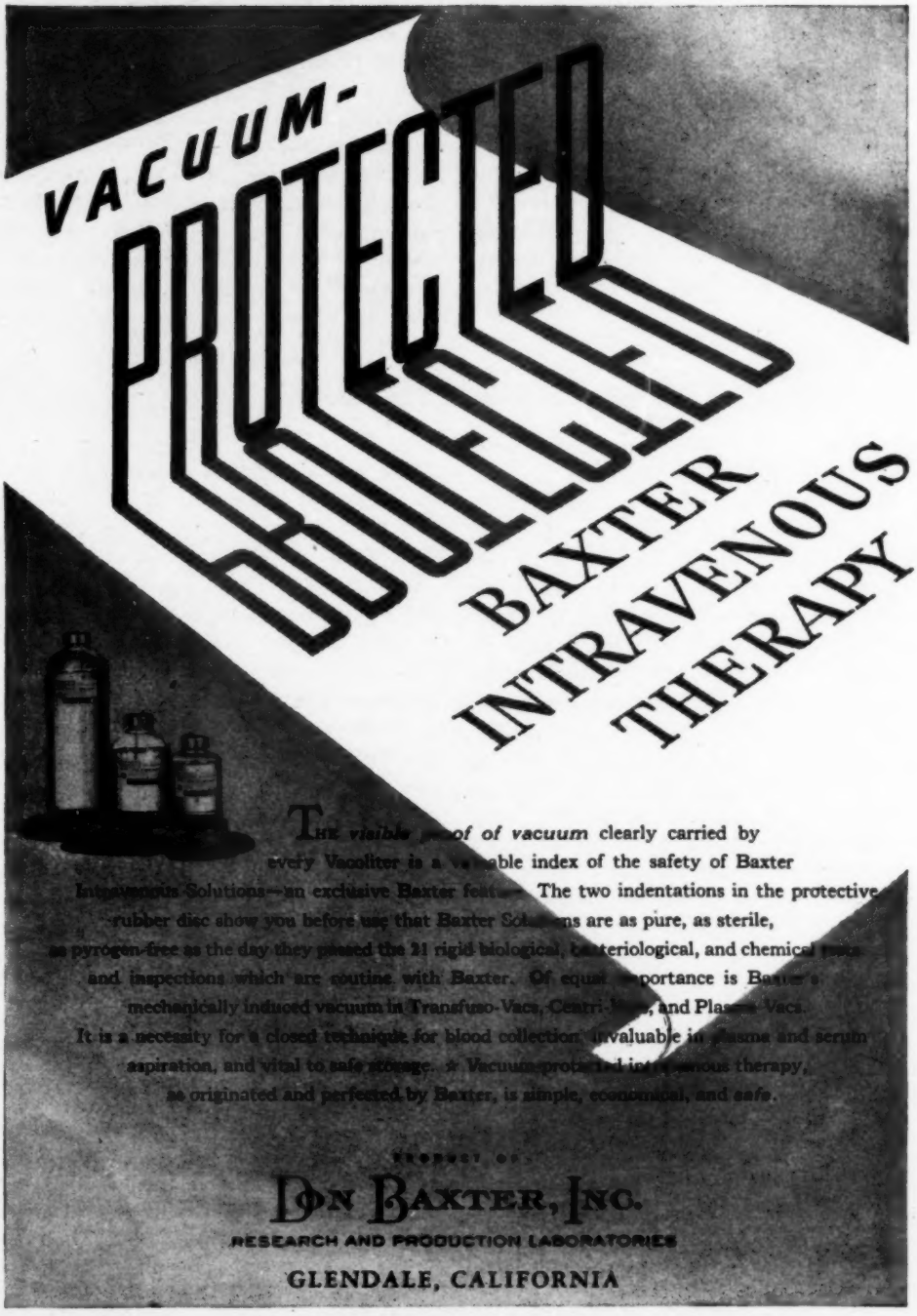
Persons rated eligible on the Medical Officer examination of 1941 need not file applications again unless they consider that they now possess qualifications for eligibility in a higher grade or different option.

Further information and application forms may be obtained at first- and second-class post offices, Civil Service Regional Offices, and the Commission in Washington, D. C.

APPEAL FOR RUSSIA

Russian War Relief, which is sending American medical textbooks to Russian schools training surgeons and doctors for the front lines, has issued a new appeal for contributions of medical literature.

The appeal was in response to requests from the Russian Society for Cultural Relations with Foreign Countries. Russian officials point out that many Soviet schools of medicine were evacuated thousands of miles to Central Asia and the Urals from Kharkov, Kiev and other occupied cities. In most cases libraries had to be left behind. The Kiev Medical Institute, cited as one example, was moved to Chelyabinsk in the Urals, 1300 miles away. The Kharkov Medical Institute, whose faculty and student body were evacuated as the Reichswehr battered at the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city's gates, is now at Chkalov, on the Ural River.

Many of the books sent from America to these and other medical schools were contributed by doctors and medical associations from all parts of the United States. They range in subject from child development to neuroses in war.

Inquiries or gifts of medical books should be sent to Russian War Relief, Inc., 11 East 35 Street, New York, 16, N. Y. A complete list of the books needed in the Soviet Union will be sent upon request. Donors may attach to their contributed books notes which will be forwarded to Russian medical libraries receiving the books.

MISCELLANY

SWEAT LOSS

In seasons and regions of great heat and high humidity, profuse perspiration is a prostrating, although expected, phenomenon. Fluids of various kinds are thirstily imbibed to replace loss through excessive perspiration, without thought of whether the ingested liquids really replaced the lost fluids. Greater relief could doubtless be attained if the physiology and chemistry of sweating were better analyzed and realized.

Sweat is a saline acid solution which may be shed at the rate of a liter an hour under trying cricumstances. It contains basic salts, especially sodium and potassium chloride, of which several grams may be lost on a hot, humid day. The acidity of sweat is largely determined by its content of lactic acid, which may be present in large amounts. Nitrogenous substances are also excreted by sweat, and such excretion has been known to reach a total of several grams of nitrogen per day. Excessive sweating may result in the elimination of more alkaline chlorides by the skin than by the kidneys and tends to result in dehydration through such loss of salt and water. Thus a physiologic process can lead to collapse or to severe muscle cramps, which can, however, be relieved or averted by drinking not water but saline solution.

Recently another important metabolic loss has been reported in cases of profuse perspiration. Water-soluble vitamins are excreted by sweat and excessive perspiration may cause an undue loss of such vitamins. It has already been demonstrated that ascorbic acid, thiamin, riboflavin, niacin, and pantothenic acid may all be eliminated in perspiration. As much as 10 per cent of some of these vitamins may be lost through this avenue of excretion. This is not a negligible amount if the diet is not optimal or if there is a protracted period of heat, as in tropical regions.

It must be obvious that in the intense heat of summer or in the tropics it is not enough to drink extra water to replace the loss incurred through sweating. Mineral loss, particularly sodium and potassium chloride, must be replaced. It now also seems that the vitamin intake should be increased in certain instances to allow for losses sustained when sweating is excessive. —*N. Y. St. J. Med.*

RULE CHANGES OF AN AMERICAN BOARD

The annual meeting of the Board was held at Pittsburgh, Pennsylvania from May 20 to May 25, 1943, at which time one hundred and eight candidates were certified.

A number of changes in Board regulations and requirements were put into effect. Several of these changes are designed to broaden the requirements for candidates in Service. Examples are the allowance of a stipulated amount of credit toward special training requirements for men in Service and assigned to general surgical positions, special training allowances on a preceptorship basis for men assigned to obstetrical or gynecological duties in military hospitals and working under the supervision of Diplomates or recognized obstetrician-gynecologists, as well as credit toward the "time in practice" requirement of the Board to be allowed for time in military service.

The Board will no longer require a general rotating internship, but will now accept a one year interne service, although the rotating internship is preferable. Such services must be in institutions approved by the Council on Medical Education and Hospitals of the A.M.A. Lists of such institutions are published regularly in the Educational Number of The Journal of the A. M. A.

The privilege of reopening applications by candidates who have been declared ineligible has been extended to two years from the date of filing the application, instead of one year.

The Board has ruled temporarily to excuse

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HER SON is in the infantry—and she knows that he can get the "job" done quicker and be home sooner if materiel is not lacking. Hence, swapping glamour for guns she takes her place in the war effort. But she has a private fight. She's at the age when she wonders if she can keep fit—physically as well as emotionally.

Clinical records show that today loss of time because of menopausal distress is largely unnecessary. Such symptoms can be relieved by adequate therapy with natural or synthetic estrogens.

Both Amniotin (natural estrogenic substance) and Diethylstilbestrol Squibb (synthetic estrogen) are available in dosage forms for oral and hypodermic administration. Diethylstilbestrol is lower in cost and, in contrast to natural estrogens, is only slightly less effective orally than intramuscularly. However, its high potency necessitates cautious use and indicates the advisability, in some instances, of building up the estrogenic level with Amniotin by injection and then, of maintaining therapy with small oral doses of Diethylstilbestrol.

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men in military service from the submission of case records at the stipulated examination times, thereby permitting them to proceed without further delay with the Board examinations. This does no obligate the Board, however, to waive the case record requirement for such candidates. Plans have been made to provide similarly for Servicemen upon their eventual discharge from the Armed Forces, and to permit the greater use of operations done while in residency or in civilian practice before the War.

The next Part I examination of the Board (written paper and submission of case records) will be held on Saturday afternoon, February 12, 1944, at a place convenient to the location of the candidate, whether he be in civilian or military life. Applications must be in the Office of the Secretary by November 15, 1943, ninety days in advance of the examination date. The time and place of the Spring 1944 (Part II) examination will be announced later.

Prospective applicants or candidates in military service are urged to obtain from the Office of the Secretary, a copy of the "Record of Professional Assignments for Prospective Applicants for Certification by Specialty Boards" which will be supplied upon request. This record was compiled by the Advisory Board for Medical Specialties and is approved by the offices of the Surgeons-General, having been recommended to the Services in a circular letter, No. 76, from the War Department Army Service Forces, and referred to as the Medical Officers Service Record. These will enable prospective applicants and candidates to keep an accurate record of work done while in military service and should be submitted with the candidate's application so that the Credentials Committee may have this information available in reviewing the application.

Applications and BULLETINS of detailed information regarding the Board requirements will be sent upon request to the Secretary's Office, 1015 Highland Building, Pittsburg, Pennsylvania.

MEDICAL COURSE INSTRUCTORS NAMED

Dr. W. L. Prothro, director of the City-County Health Unit, today named 11 instructors who will assist him in teaching a survey course in medicine during the second semester of the sum-

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**Proc. Soc. Exp. Bio. and Med., 1934, 32, 241-245* ***Laryngoscope, 1935, XLV, No. 2, 149-154*

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mer session at the College of Mines. Others will be named soon.

Dr. Prothro will give the introductory lectures and will also speak on public health work, the effects of immunization and deduction in the prevention of disease, and physical defects.

Dr. J. Mott Rawlings will lecture on anatomy, comparative anatomy embryology, and the pathology and hygiene of the different systems of the body. Dr. W. E. Vandevere will speak on the physiology and hygiene of the eye. Dr. Frank Schuster will lecture on the ear, nose and throat. Dr. J. E. Hymes will speak on dental work.

Dr. L. O. Dutton will lecture on malnutrition and related defects and will discuss the use of vitamins in prevention of disease. He will also lecture on acute communicable diseases.

Dr. Mildred Murray will speak on health problems of girls and Dr. J. W. Laws will lecture on tuberculosis. Dr. Orville Egbert will speak on X-ray, physiotherapy and diathermy. Dr. E. J. Cummings will lecture on surgery.

Harold Tillman, sanitary engineer of the City-County Health Unit, will speak on sanitation. Dr. Walter Knox will give a survey of healing practice.

All the lectures will give special emphasis to the health problems of school children. Dr. Prothro said.

The course is part of a series of three courses being offered for teachers during the college's summer session.

Registration for the second term of summer school will open Thursday.

—*El Paso Herald-Post*

NEEDED—A POPULATION POLICY

It is being pointed out by anthropologists and sociologists that "the effective fertiliy of the American people is likely to fall below the level required to maintain a stationary population." This is not the case with Japan and Panunzio of the University of California points out in the April *Scientific Monthly* that even if we win the present war against Japan "we may, in the next generation, be obliged to confront a nation with an even greater manpower than it now possesses."

It seems that by 1970 Japan's total population will probably increase by about thirty millions, while that of the United States will in-

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crease by only eighteen millions. "And," Panunzio goes on. "since the age structure of the two nations is markedly different, Japan will have an appreciably greater proportionate increase in manpower than will the United States. Any loss of births at present on the part of the United States will, therefore, be far more serious than that which Japan can experience. In view of these facts, the United States and Japan will face a manpower situation somewhat similar to that which France and Germany faced in 1940. This statement is intended to create alarm, but even more to stress the full import of the situation." —*Med. Times*

AMERICAN CONGRESS OF PHYSICAL THERAPY

The twenty-second annual scientific and clinical session is to be held September 8, 9, 10 and 11, 1943, inclusive, at the Palmer House, Chicago. The annual instruction course will be held from 8:00 to 10.30 A. M., and from 1:00 to 2:00 P. M. during the days of September 8, 9 and 10, and will include a round table discussion group from 9:00 to 10:30 A. M., Thursday, September 9. The scientific and clinical sessions will be given on the remaining portions of these days and evenings. A feature will be an hour demonstration showing technic from 5:00 to 6:00 P. M. during the days of September 8, 9 and 10. All of these sessions will be open to the members of the regular medical profession and their qualified aids. For information concerning the instruetion course and program of the convention proper, address the American Congress of Physical Therapy, 30 North Michigan Avenue, Chicago, Illinois.

ALCOHOLISM

1. Chronic alcoholic addicts have a condition known as beriberi, pellagra, riboflavin deficiency, labelled "alcoholic starvation syndrome."

2. These patients, in addition to nourishing, vitamin rich food, need additional amounts of synthetic vitamins, namely, thiamin hydrochloride, niacin, and riboflavin in relatively large doses.

3. Commercial drug companies do not manufacture a B-complex preparation containing adequate dosage of nicotinic acid. The preparation we have used was compounded locally from synthetic niacin, thiamin chloride and riboflavin.

4. The avitaminosis encountered in alcoholic addicts far overshadows any other factor from a therapeutic standpoint.

5. Stimulation therapy proves more efficacious than sedatives in the acute "hangover" stage of the disease.

6. Alcoholic addicts should be considered as physiological problems, rather than psychiatric problems as has been too often the case in the past.

7. Social readjustment should be attempted as a follow-up course of therapy with psychotherapy being called into play as a follow-up measure only.

8. Institutions other than jails, asylums or almshouses should be established to treat alcoholic addicts.

9. There is no so-called "cure" for alcoholic addiction. The patient must have formed a desire to quit before any treatment has a chance of succeeding.

10. "Alcoholic Anonymous" organizations should be given a chance to reorganize the patient's social life. —*Jo. M.S.M.S.*

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